UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,275	04/09/2001	Suzanne Walker	4555-105 US	7235

7590 06/16/2004

Diane Dunn McKay, Esq.
Mathews, Collins, Shepherd & Gould, P.A.
Suite 306
100 Thanet Circle
Princeton, NJ 08540

EXAMINER	
NASHED, NASHAAT T	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/829,275	WALKER ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-146* is/are pending in the application.

4a) Of the above claim(s) *3-146* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/22/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-146 are pending.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 and 2, drawn to a crystalline composition of MurG (membrane-associated UDP-glycosyltransferase), classified in class 435, subclass 193.

II. Claims 3-10, drawn to a three-dimensional structure of MurG and a model thereof, classified in class 434, subclass 324+.

III. Claims 39-44, drawn to a computer readable medium, classified in class 369.

IV. Claims 45-51, and 117-132, drawn to to a method of identifying potential inhibitor of MurG, classified in class 702, subclass 19.

V. Claims 133 and 134, drawn to a modeled structure of MurG, classified in class 369.

VI. Claims 135-142, drawn to a composition of modulator of MutG activity, Classification is unknown. Since the specification has not exemplified a modulator of activity, the examiner can't classify this invention.

VII. Claims 143-145, drawn to a modeling method of a MurG, classified in class 702, subclass 19.

VIII. Claim 146, drawn to a method of determining the three dimension structure of a MurG of unknown three dimensional structure, classified in class 435, subclass 15.

The inventions are distinct, each from the other because of the following reasons:

Inventions I, and those of inventions II-VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case:

(a) The crystalline composition of invention I, and the three-dimensional structure of invention II are not disclosed as capable of use together;

(b) The crystalline composition of invention I, and the computer readable medium of invention III are not disclosed as capable of use together;

(c) The crystalline composition of invention I is not utilized by any of the methods of invention IV and VII; and

(e) The crystalline composition of invention I, and the modulator of MurG of invention VI are independent chemical entities and require independent searches in the patent and non-patent literature.

Inventions I, and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the crystal can be used in other methods such as in a method for the purification of MurG.

Invention II, and those of inventions III, V, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the inventions have different functions.

Inventions II, and those IV, VII, and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the three-dimensional structure can be used in other methods such as the different methods of inventions IV, VII and VIII.

Invention II, and V, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the inventions have different functions.

Inventions III, and those IV, VII, and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the computer readable medium is used in three different methods.

Invention III, and V, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the inventions have different functions.

Invention IV, and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In

the instant case, the method of invention IV does not utilize the modeled structure of invention V.

Inventions IV, and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the inhibitor can be identified by other method such as screening method in solution.

Invention IV, VII, and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are independent methods having different steps and products.

Inventions V, and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different function.

Inventions V and VII are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the modeled structure may be obtained by a different method utilizing the three dimensional structure of other glycosyltransferase.

Inventions V, and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the modeled structure of invention V is not utilized by the method of invention VIII.

Invention VI, and those of inventions VII and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the composition of invention VI is not utilized by the method of invention VII and VIII.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with Diane McKay on June 4, 2004 a provisional election was made with traverse to prosecute the invention of I, claims 1 and 2. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-146 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the

color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

New corrected drawings are required in this application because the color scheme in the drawing does not reproduce well in black and white drawing, e.g., purple and green are black, and therefore, the examiner could not comprehend the figure description and other parts of the specification referring to the colored drawings. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

The disclosure is objected to because of the following informalities: The title of the invention is more than 500 characters. 37 CFR 1.72 (a) states: The title of the invention may not exceed 500 characters in length and must be as short and specific as possible. Characters that cannot be captured and recorded in the Office 's automated information systems may not be reflected in the Office 's records in such systems or in documents created by the Office. Unless the title is supplied in an application data sheet (§ 1.76), the title of the invention should appear as a heading on the first page of the specification.

Appropriate correction is required.

The following title is suggested: Crystal Structure of *Escherichia coli* Membrane-associated UDP-glycosyltransferase and Uses thereof.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 2 are directed to all possible crystals of any UDP-glycosyltransferase (MurG) from *E. coli* and any biological source, respectively. The specification, however, only provides a single representative species of these crystals encompassed by these claims. The specification teaches the crystallization of *E. coli* MurG of SEQ ID NO: 1, which comprises the MurG attached to histadine tag at the C-terminus, and obtaining a triclinic crystal in space group P1 with cell unit dimension a = 60.613 Å, b = 66.356 Å, and c = 67.902 Å; and α = 64.294, β = 83.520, γ = 65.448°. There is no disclosure of any particular teaching on how to change the crystallization conditions to obtain any MurG protein crystal with the change in the protein sequence, or any other crystal form. The specification also fails to describe additional representative species of these crystals by any identifying structural characteristics or properties other than the cell dimension, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. The insertion of SEQ ID NO: 1, the space group, and cell unit dimension in claims 1 and 2 would obviate this.

Claims 1 and 2 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to *E. coli* MurG triclinic crystal of SEQ ID NO: 1, which comprises the MurG attached to histadine tag at the C-terminus, in space group P1 with cell unit dimension a = 60.613 Å, b = 66.356 Å, and c = 67.902 Å; and α = 64.294, β = 83.520, γ = 65.448°. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible crystals of MurG proteins, which formed under any crystallization conditions. Factors to be considered in determining whether undue experimentation is required are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any crystal of MurG protein from any biological source. The specification provides guidance and examples in the form of an assay to obtain the MurG protein of SEQ ID NO: 1, crystallize the protein under the conditions described in the paragraph bridging pages 186 and 187, and determine the three dimensional structure pg the MurG protein by the X-ray diffraction method (example 1). While molecular biological techniques and genetic manipulation to make any MurG protein having any amino acid sequence are

known in the prior art and the skill of the artisan are well developed, knowledge regarding the crystallization conditions to obtain a suitable crystal for structure determination by the X-ray diffraction method is lacking. Thus, searching a crystallization conditions for any MurG protein is well outside the realm of routine experimentation and predictability in the art of success is extremely low. Applicants themselves recognize the unpredictability of growing crystals and write:

> "It is well known in the protein crystallographic art that obtaining crystals of quality sufficient for determining the structure of a protein is unpredictable", see page 4, paragraph 2.

The amount of experimentation to identify a crystallization conditions is enormous. Applicants should be reminded that growing protein crystals to a suitable size that diffracts X-ray is not amenable to scientific investigation. It relies mostly on trial and error. A minor a change in an amino acid sequence such as a conservative mutation may have a profound effect on the crytallizability of a protein under a given crystallization conditions. In many instants, a crystal may be obtained, but it would diffract X-ray poorly. The formation of MurG crystal complex with an agent that binds to MurG protein is highly unpredictable. There are two known methods for obtaining a crystal complex with a compound that binds to the MurG protein. The first is to include in the crystallization conditions a compound that binds to MurG. In many instants, the compound-MurG protein complex crystal may not form and would require new screening for new crystallization conditions, which would produce a crystal suitable for X-ray diffraction. Also, the crystal may not be isomorphous to the underivatized crystal. The second method is socking underivatized crystals in the mother liquor from which the crystal has grown containing the desired ligand. Once again, that may lead to the destruction of the crystal or recrystallization of the protein. Since routine experimentation in the art does not include screening vast numbers of crystallization condition which may include going out to space to attempt growing crystals in microgravity environment where the expectation of obtaining the desired crystal is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the exact crystallization conditions and the amino acid sequence which is being crystallized. Without such guidance, the experimentation left to those skilled in the art is undue.

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 2 contain the undefined abbreviation "MurG" which renders the claims indefinite.

The claims are free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N Nashed

Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1652